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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/069,357	05/09/2002	Bernd Ibscher	0273-0009	1386

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EXAMINER	
KISHORE, GOLLAMUDI S	
ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 02/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/069,357	IBSCHER ET AL.	
	Examiner	Art Unit	
	Gollamudi S Kishore, Ph.D	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 September 0504*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment dated 9-15-04 is acknowledged.

Claims included in the prosecution are 24-55.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 24-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over DE 4021082 cited in the previous action.

As discussed above, DE discloses skin treatment compositions containing liposomal gel. The gels contains a phospholipid, phosphatidylcholine (10 %), alcohol (0.1-20 %), inositol (0.1 to 10 %) and the rest water. The alcohol is either a propylene glycol or glycerin or mixtures thereof. The (note the abstract, page 4, line 56 through page 7, line 34, Examples and claims). DE does not teach all of the claimed ranges for the components. In the absence of showing unexpected results, it is deemed obvious to one of ordinary skill in the art to vary the ratios taught by DE to obtain the best possible results with the guidance provided by DE. DE does not appear to teach the additional amounts of glycerol or ethanol as in instant claims. However, in the absence of showing the criticality, in view of its teachings of the use of mixtures, it is deemed obvious to one of ordinary skill in the art

to manipulate the basic teachings of DE to obtain the best possible dissolution of an active agent and to obtain the best possible results. Such a skill is within the skill of the art. DO does not appear to teach the use of buffers. However, since the appropriate pH conditions are desirable to prevent the adverse side effects of a composition on the skin when used topically, it is deemed obvious to one of ordinary skill in the art to use buffers. Although the method of preparation described by DE is by mixing the components together it does not appear to teach the mixing to be done in an inert atmosphere. However, it is within the skill of the art to recognize that phospholipids are susceptible to oxidation and therefore, the mixing has to be done in an oxygen free atmosphere if the phospholipids are unsaturated.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that DE teaches and claims skin treatment agents containing a bilayer source, salts of organic acids, alcohol, a stabilizer and lipids and that the present invention does not teach the use of salts of organic acids, nor of lipids nor a stabilizer within the asserted meaning of those terms in DE. Furthermore, applicant argues that DE teaches the use of urea and or monosaccharides. This argument is not found to be persuasive since instant claims do not exclude the other components taught by DE. Furthermore, instant claim 24 recites, "one or more additives having pharmaceutical activity or cosmetic action". Applicant's arguments that DE teaches away from the use of phospholipids comprising greater than 10 % of the formulation because of the danger of auto-oxidation. This argument is not found to be persuasive since instant lower limit is just a little over 10 % and the prior art teaches the

upper limit of 10 %. An artisan would be motivated to manipulate the levels of the lipids in DE within reasonable limits to obtain the best possible results. Applicant's arguments with regard to the disadvantages of liquification of the gels when readily soluble substances such as diphenhydramine are not found to be persuasive for the above reason, i.e., the lower limit of the phospholipid in instant invention and the upper limit in DE are around the same amount.

8. Claims 24-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over DE 4021082 cited above in combination with EP 0158 444 cited in the previous action or DE 195 20 659 (cited on page 2 of the specification) or Boni (5,820,848 also cited on page 2 of the specification).

The teachings of DE have been discussed above. What are lacking in the teachings of DE are the explicit teachings of higher amounts of phospholipid and the use of a buffer and the use of an inert atmosphere to prepare the phospholipid formulations.

EP discloses compositions containing 45 % phospholipids (unsaturated lecithin or saturated DPPC), 36 % ethylene glycol or propylene glycol and 0.9 % glucose. EP also teaches the use of phosphate buffer of pH 7.4 and the preparation is done in N2 atmosphere. The drugs taught are insulin. According to EP, the preparations have high drug entrapment ratios (abstract, page 5, lines 2425, page 10, lines 11-22; page 12, lines 18-31; page 13, line 34 through page 14, line 34; Examples, examples 16 and 18 in particular).

The reference of DE (659) teaches compositions containing 5-35 percent of phospholipid. The compositions also contain a mixture of di or trihydric alcohol with ethanol (see page 2 of instant specification).

Boni teaches phospholipid gels containing 99 percent of DPPC. The compositions also contain alcohols such as ethanol and glycerol (abstract, col. 10 and examples, example 2 in particular).

It would have been obvious to one of ordinary skill in the art to increase the amount of the phospholipid in DE with a reasonable expectation of increasing the amount of active agent which is entrapped since EP shows the use of higher amounts of phospholipids and increased amounts of entrapped agent with these higher amounts and both DE and Boni show the routine use of higher amounts of phospholipids in gel formulations. It would have been obvious to one of ordinary skill in the art to use appropriate buffers when used in combination with labile drugs such as insulin and use an inert atmosphere while preparing the compositions as evident from EP and from the guidance provided by EP with a reasonable expectation of success. The use of hydrogenated phosphatidylcholine instead of unsaturated compound, with a reasonable expectation of success, would have been obvious to one of ordinary skill in the art since EP advocates such a use.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that DE and EP are not combinable since DE is directed to skin treatment compositions and EP teaches pro-liposomal compositions comprising phospholipids capable of forming liposomes when agitated in excess water and for use

as drug carrier. This argument is not persuasive. First of all, irrespective of what the formulation is used for, EP deals with liposome preparations and the use of buffers when appropriate and the method of formation of bilayer structures and these will be the same irrespective of the intended use. Secondly, applicant is incorrect in stating that EP is just meant as a drug carrier. EP is meant for both internal and external use as evident from page 9, lines 19-21. Finally, it should be pointed out that instant claim 24 itself recites 'cosmetic or pharmaceutical additives'.

1. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S Kishore, Ph.D whose telephone number is

(571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM; alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gollamudi S Kishore, Ph.D
Primary Examiner
Art Unit 1615

GSK